Complete Summary

GUIDELINE TITLE

Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents.

BIBLIOGRAPHIC SOURCE(S)

Panel on Clinical Practices for Treatment of HIV Infection. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Bethesda (MD): Department of Health and Human Services (DHHS); 2004 Oct 29. 110 p. [287 references]

GUIDELINE STATUS

This is the current release of the guideline. It was last updated on October 29, 2004.

These guidelines generally represent the state of knowledge regarding the use of antiretroviral agents. However, as the science rapidly evolves, the availability of new agents and new clinical data may rapidly change therapeutic options and preferences. The guidelines are therefore updated frequently by the Panel, which meets monthly by teleconferencing to make ongoing revisions as necessary. All revisions are summarized and highlighted on the AIDSinfo Web site. Proposed revisions are posted for a public comment period, generally for 2 weeks, after which comments are reviewed by the Panel prior to finalization. Comments can be sent to aidsinfowebmaster@aidsinfo.nih.gov.

Status information regarding this guideline is available from the AIDSinfo Web site, telephone (800) 448-0440, fax (301) 519-6616; TTY (888) 480-3739.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

- Human immunodeficiency virus (HIV) infections (including asymptomatic, established, and acute HIV)
- Acquired immunodeficiency syndrome (AIDS)

GUIDELINE CATEGORY

Management
Treatment

CLINICAL SPECIALTY

Family Practice
Infectious Diseases
Internal Medicine
Obstetrics and Gynecology
Pediatrics
Preventive Medicine

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To use the advances in current understanding of the pathogenesis of human immunodeficiency virus (HIV) in the infected person to translate scientific principles and data obtained from clinical experience into recommendations that can be used by the clinician and patient to make therapeutic decisions

TARGET POPULATION

Adults and adolescents infected with human immunodeficiency virus (HIV)

These guidelines focus on treatment for adults and adolescents. Separate guidelines outline how to use antiretroviral therapy for such populations as pregnant women, pediatric patients, and health care workers with possible occupational exposure to HIV. There is a brief discussion of the management of women in reproductive age and pregnant women in this document. However, for more detailed and up-to-date discussion on this and other special populations, the Panel defers to the designated expertise outline by panels that have developed these guidelines.

INTERVENTIONS AND PRACTICES CONSIDERED

1. The use of testing for plasma human immunodeficiency virus ribonucleic acid (HIV RNA) levels (viral load) and $CD4^+$ T cell count in guiding decisions for therapy
2. Evaluation before initiating therapy, including complete history and physical, complete blood count, chemistry profile (including serum transaminases and lipid profile); additional evaluation to prevent opportunistic infections, as needed
3. Testing for antiretroviral drug resistance, including genotyping and phenotyping assays
4. Approaches to improve adherence to antiretroviral therapy including:
    - Patient-related strategies
    - Clinician and health team-related strategies
    - Regimen-related strategies
    - Directly observed therapy
    - Patient education
    - Pharmacist-based adherence encounters/clinics
5. Discontinuing and/or interrupting therapy
6. Criteria for changing therapy and alternative therapeutic options
7. Prevention counseling, including assessment and documentation of patient's knowledge and understanding of the means of HIV transmission, the patient's HIV transmission behaviors since last encounter with health care provider, and discussion of strategies to prevent transmission
8. Antiretroviral agents:
    - Nucleoside analogue reverse transcriptase inhibitors (NRTIs):
        - Zidovudine (ZDV; AZT; Retrovir®)
        - Didanosine (ddI; dideoxyinosine; Videx®)
        - Zalcitabine (ddC; dideoxycytidine; Hivid®)
        - Stavudine (d4T; Zerit®)
        - Lamivudine (3TC, Epivir®)
        - Abacavir (ABC; Ziagen®)
        - Tenofovir disoproxil fumarate (TDF) (Viread®)
        - Emtricitabine (Emtriva™)
    - Non-nucleoside reverse transcriptase inhibitors (NNRTIs):
        - Delavirdine (DLV; Rescriptor®)
        - Efavirenz (Sustiva®)
        - Nevirapine* (NVP; Viramune®)

          *Note from the National Guideline Clearinghouse: On January 19, 2005, the U.S. Food and Drug Administration (FDA) issued a public health advisory about recent safety-related changes to the nevirapine (Viramune®) label and about appropriate use of HIV triple combination therapy containing nevirapine. The Indications and Usage section now recommends against starting nevirapine treatment in women with CD4+cell counts greater than 250 cells/mm3 unless benefits clearly outweigh risks. This recommendation is based on a higher observed risk of serious liver toxicity in patients with higher CD4 cell counts prior to initiation of therapy. See the FDA Web site for more information.

    - Protease inhibitors (PIs):
        - Indinavir (Crixivan®)

        - Nelfinavir (Viracept®)
        - Fosamprenavir (Lexiva™)
        - Ritonavir (Norvir®)
        - Saquinavir (hard gel capsule, Invirase®, and soft gel capsule, Fortovase®)
        - Amprenavir (Agenerase®)
        - Lopinavir/Ritonavir (Kaletra®)
        - Atazanavir (Reyataz™)
    - Fusion inhibitor (FIs)
        - Enfuvirtide (Fuzeon®)

          Note: Until the results of further clinical studies are known, FIs should be reserved for patients who have failed initial regimens.

MAJOR OUTCOMES CONSIDERED

- Viral load
- Immunologic function
- Adherence to treatment
- Therapy-associated adverse effects
- Quality of life
- Human immunodeficiency virus (HIV)-related morbidity and mortality

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Categories reflecting the quality of evidence supporting the recommendations:

I. At least one randomized trial with clinical results
II. Clinical trials with laboratory results
III. Expert opinion

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Strength of Recommendation

A. Strong
B. Moderate
C. Optional
D. Should usually not be offered
E. Should never be offered

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Note from the National Guideline Clearinghouse (NGC) and the Department of Health and Human Services: This guidelines revision represents a major rewriting of the document to improve its organization and readability. The tables are updated with the most current available information. Following are the major changes that have been made to the March 28, 2004, version of the guidelines, followed by a summary of the guidelines. Please refer to the original guideline document at the AIDSinfo Web site for further details.

Changes in Recommendations

When to start?

For asymptomatic treatment-naïve patients with CD4+ T cell count >350 cells/mm^3, the viral load recommendation to defer or to consider therapy has been increased from 55,000 to 100,000 copies/mL. This is based on more recent data supporting human immunodeficiency virus ribonucleic acid (HIV RNA) level of >100,000 copies/mL being a stronger predictor for disease progression than >55,000 copies/mL, though even at these CD4 and viral load levels, the risk of disease progression is still relatively low. Most experienced clinicians will defer therapy with quarterly clinical and laboratory evaluation.

What to start with?

- Stavudine has been moved from "preferred" to "alternative" due to increasing reports of stavudine-associated toxicities.
- Tenofovir plus lamivudine (or emtricitabine) is now recommended as a 2-nucleoside reverse transcriptase inhibitor (NRTI) backbone for both non-nucleoside reverse transcriptase inhibitor (NNRTI)- and protease inhibitor (PI)-based regimens. Previously, this recommendation was limited to NNRTI-based regimens only.
- Emtricitabine is now included as an option for part of a preferred or alternative 2-NRTI backbone.

Additions to the Guidelines Document

- Special Populations section: Discussions on special considerations for antiretroviral therapy in the following patient populations are added to this document:
    - HIV-infected adolescents
    - Injection drug users
    - Hepatitis B/HIV coinfected patients
    - Hepatitis C/HIV coinfected patients
    - HIV patients with tuberculosis
- Discussion on Discontinuation or Interruption of Antiretroviral Therapy
- The following tables:
    - "Probability of progressing to AIDS or death according to CD4 cell count, viral load, and sociodemographic factors" reproduced with permission from Lancet 2002
    - "Predicted 6-month risk of AIDS according to age and current CD4 cell count and viral load, based on a Poisson regression model" reproduced with permission from AIDS 2004
    - "A compilation of 48-week treatment outcome data from selected clinical trials of combination antiretroviral therapy in treatment-naïve individuals"
    - "Antiretroviral therapy associated adverse effects and management recommendations"

Deletion from the Guidelines Document

What not to use?

Hydroxyurea: Hydroxyurea has been removed from this list as it is the opinion of the Panel that discussions in the guidelines should limit themselves to commentary on U.S. Food and Drug Administration (FDA)-approved agents that are indicated for the treatment of HIV infection. Hydroxyurea, though used by some as adjunctive therapy to antiretroviral agents, is not considered, by itself, an antiretroviral agent, and thus will not be discussed in this guidelines document.

Summary of Guidelines

The following provides a summary of the major recommendations presented in the guideline document. The reader is directed to the original guideline document for a detailed discussion of each of the topics presented below.

Antiretroviral therapy for treatment of human immunodeficiency virus type 1 (HIV-1) infection has improved steadily since the advent of combination therapy in 1996. More recently, new drugs have been approved, offering added dosing convenience and improved safety profiles, while some previously popular drugs are being used less often as their drawbacks become better defined. Resistance testing is used more commonly in clinical practice and interactions among antiretroviral agents and with other drugs have become more complex.

The Panel on Clinical Practices for Treatment of HIV (the Panel) develops these guidelines which outline current understanding of how clinicians should use antiretroviral drugs to treat adult and adolescents with HIV infections. The Panel considers new evidence and adjusts recommendations accordingly. The primary areas of attention and revision have included when to initiate therapy, which drug combinations are preferred and which drugs or combinations should be avoided, and means to continue clinical benefit in the face of antiretroviral drug resistance. In contrast, some aspects of therapy, while important, have seen less rapid data evolution and thus fewer changes, such as medication adherence. Yet other topics have warranted more in-depth attention by separate guidelines groups, like the treatment of HIV during pregnancy.

Key Clinical Questions Addressed By Guidelines

For ease of use, the original guideline document is organized so as to answer the following series of clinical questions clinicians are most likely to face in making treatment decisions:

- When should therapy be started in patients with established asymptomatic infection? The Panel reaffirms the desirability of initiating therapy before the CD4 cell count falls below 200 cells/mm^3. In addition, there are no data documenting added value in treating before the count falls below 350 cell/mm^3, but some clinicians opt to consider treatment in patients with CD4 count >350 cell/mm^3 and HIV RNA >100,000 copies/mL. A review of the literature on this issue can be seen in the "When to Treat: Indications for Antiretroviral Therapy" section in the original guideline document.
- Which regimens are preferred for initial therapy? The Panel continues to select several regimens as preferred, while appreciating that patient or provider preferences or underlying comorbidities may make an alternative regimen better in such instances. The Panel recommends that an initial regimen contain two nucleoside/nucleotide reverse transcriptase inhibitors

(NRTI) and either a non-nucleoside reverse transcriptase inhibitor (NNRTI) or a ritonavir-boosted or unboosted protease inhibitor (PI).

- What drugs or drug combinations should not be used? The Panel notes that certain drugs are so similar, for example, lamivudine and emtricitabine, that they should not be combined. Others have additive or synergistic toxicity, such as stavudine with didanosine, and should generally be avoided. Still others have intracellular interactions that decrease their antiviral activities, notably zidovudine with stavudine, and should thus be avoided.
- What are some limitations to the safety and efficacy of antiretroviral therapy? The Panel notes the high degree of medication adherence with all antiretroviral (ARV) regimens needed to prevent the selection of drug resistance. It also appreciates that short term and, even more concerning, longer term toxicity may limit the duration of treatment needed in what can be seen as a chronic disease. Finally, drug interactions among the antiretroviral drugs and with other necessary drugs are challenging and require special attention in prescribing and monitoring.
- What is the role of resistance testing in guiding therapy decisions? Resistance testing continues to be an important component of optimizing drug selection after treatment failure. However, its role in previously untreated persons is less clear. The Panel recognizes that there is a growing sense that such applications are of value, but little evidence exists to guide such use.
- What are the goals of therapy in treatment experienced patients? When possible, suppression of viremia to less than detection limits remains the goal of therapy. When this is not possible, the Panel recommends maintenance of even partial viremic suppression by selection of an optimal regimen based on resistance testing results. Either way, the ultimate goals are to prevent further immune deterioration and to avoid HIV-associated morbidity and mortality. The Panel recommends against complete antiretroviral cessation in late failure as this has resulted in rapid progression to acquired immune deficiency syndrome (AIDS) and death.
- Are there special populations which may require specific considerations when using antiretroviral therapy? The Panel recognizes that there are subgroups of patients where specific considerations are critical when selecting and monitoring antiretroviral therapy, in order to assure safe and effective treatment. The Panel addresses some important antiretroviral related issues for these special populations, which include patients with acute HIV infection, HIV-infected adolescents, injection drug users, women of child bearing potential and pregnant women, and those with hepatitis B, hepatitis C, or tuberculosis coinfections.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

Recommendations are based upon expert opinion and scientific evidence. When appropriate data are not available, inconclusive, or contradictory, the recommendation is based on "expert opinion." The type of supporting evidence is identified for specific recommendations in the original guideline document.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Overall Benefits

The primary goals of antiretroviral therapy are maximal and durable suppression of viral load, restoration or preservation of immunologic function, improvement of quality of life, and reduction of human immunodeficiency virus (HIV)-related morbidity and mortality.

Specific Benefits

Potential Benefits of Deferred Therapy:

- Avoidance of treatment-related negative effects on quality of life and drug-related toxicities
- Preservation of treatment options
- Delay in the development of treatment resistance if there is incomplete viral suppression
- More time for the patient to have a greater understanding of treatment demands
- Decreased total time on medication with reduced chance of treatment fatigue
- More time for the development of more potent, less toxic, and better studied combinations of antiretrovirals

Subgroups Most Likely to Benefit

Patients with Acute HIV Infection

Preliminary data indicate that treatment of acute HIV infection with combination antiretroviral therapy has a beneficial effect on laboratory markers of disease progression. Theoretically, early intervention could decrease the severity of acute disease; alter the initial viral setpoint, which can affect disease-progression rates; reduce the rate of viral mutation as a result of suppression of viral replication; preserve immune function; and reduce the risk for viral transmission.

POTENTIAL HARMS

Overall Harms

The risks of therapy for human immunodeficiency virus (HIV) infection include adverse effects on quality of life resulting from drug toxicities and dosing constraints; the potential, if therapy fails to effectively suppress viral replication, for the development of drug resistance, which may limit future treatment; and the potential need for continuing therapy indefinitely.

Specific Harms

Potential Risks of Deferred Therapy:

- The possibility that damage to the immune system, which might otherwise be salvaged by earlier therapy, is irreversible
- The increased possibility of progression to acquired immune deficiency syndrome (AIDS)
- The increased risk for HIV transmission to others during a longer untreated period

Refer to the original guideline document for important and more detailed information regarding the potential risks of individual antiretroviral drugs, highly active antiretroviral therapy, and potential drug interactions.

Subgroups Most Likely to be Harmed

Women of Reproductive Age

In women of reproductive age, regimen selection should account for the possibility of planned or unplanned pregnancy. The most vulnerable period in fetal organogenesis is early in gestation, often before pregnancy is recognized. Sexual activity, reproductive plans, and use of effective contraception should be discussed with the patient. As part of the evaluation for initiating therapy, women should be counseled about the potential risk of efavirenz-containing regimens should pregnancy occur. These regimens should be avoided in women who are trying to conceive or are not using effective and consistent contraception. This counseling should be provided on a routine basis after initiation of therapy as well.

Pregnant Women

Pregnancy should not preclude the use of optimal therapeutic regimens. However, because of considerations related to prevention of mother-to-child-transmission and to maternal and fetal safety, timing of initiation of treatment and selection of regimens are different than for the nonpregnant adults or adolescents.

Patients with Acute HIV Infection

The potential disadvantages of initiating therapy include exposure to antiretroviral therapy without a known clinical benefit, which could result in drug toxicities, development of antiretroviral drug resistance, the need for continuous therapy, and adverse effect on quality of life.

CONTRAINDICATIONS

CONTRAINDICATIONS

Some antiretroviral regimens or components are not recommended for human immunodeficiency virus type 1 (HIV-1) infected patients due to suboptimal antiviral potency, unacceptable toxicity, or pharmacological concerns. These are summarized as follows:

- Monotherapy: Single antiretroviral drug therapy does not demonstrate potent and sustained antiviral activity and should not be used. The rare exception, though controversial, is the use of zidovudine monotherapy to prevent

perinatal HIV-1 transmission in a woman who does not meet clinical, immunologic, or virologic criteria for initiation of therapy and who has an HIV ribonucleic acid (RNA) <1,000 copies/mL. Most clinicians, however, prefer to use a combination regimen in the pregnant woman for the management of both the mother's HIV infection and in the prevention of perinatal transmission. The efficacy of zidovudine monotherapy during pregnancy to reduce perinatal transmission was identified in the Pediatric AIDS Clinical Trial Group (PACTG) 076 study. The goal of therapy in this case is solely to prevent perinatal HIV-1 transmission. Zidovudine monotherapy should be discontinued immediately after delivery. Combination antiretroviral therapy should be initiated postpartum if indicated.

- Dual nucleoside therapy: These regimens are not recommended because they have not demonstrated potent and sustained antiviral activity as compared to three-drug combination regimens. For patients previously initiated on this treatment who have achieved sustained viral suppression, it is reasonable to continue on this therapy or to add a protease inhibitor (PI) or non-nucleoside reverse transcriptase inhibitor (NNRTI) to this regimen. If the patient is to stay on a 2-nucleoside reverse transcriptase inhibitor (NRTI) regimen, the plan should be to change to a three or more drug combination if viral rebound occurs.
- 3-NRTI regimen with abacavir plus tenofovir plus lamivudine: In a randomized trial for treatment naïve patients, those randomized to a regimen consisting of abacavir + tenofovir + lamivudine had a significantly higher rate of "early virologic non-response" when compared to patients treated with efavirenz + abacavir + lamivudine. This combination should not be used as a 3-NRTI regimen in any patient.
- 3-NRTI regimen with didanosine plus tenofovir plus lamivudine: In a small pilot study, a high rate (91%) of virologic failure (defined as <2 log reduction of HIV-RNA by week 12) was seen in treatment–naïve patients initiated on this 3-NRTI regimen. This combination should not be used as a 3-NRTI regimen in any patient.
- Amprenavir oral solution in pregnant women, children <4 years of age, patients with renal or hepatic failure, and patients treated with metronidazole or disulfiram: Due to the large amount of propylene glycol used as an excipient, which may be toxic to high-risk populations.
- Amprenavir plus fosamprenavir: Fosamprenavir is the prodrug of amprenavir. There is no additional benefit, and potential additive toxicities, when using these agents together.
- Amprenavir oral solution plus ritonavir oral solution: The large amount of propylene glycol used as a vehicle in amprenavir oral solution may compete with the ethanol (vehicle of oral ritonavir solution) for the same metabolic pathway for elimination. This may lead to accumulation of either one of the vehicles.
- Atazanavir plus indinavir: Both of these PIs can cause grade 3 to 4 hyperbilirubinemia and jaundice. Additive or worsening of these adverse effects may be possible when these agents are use concomitantly.
- Didanosine plus stavudine: The combined use of didanosine and stavudine as a 2-NRTI backbone can result in a high incidence of toxicities, particularly peripheral neuropathy, pancreatitis, and lactic acidosis. This combination has been implicated in several deaths in HIV-1 infected pregnant women secondary to severe lactic acidosis with or without hepatic steatosis and pancreatitis. In general, a combination containing didanosine and stavudine should be avoided unless other 2-NRTI combinations have failed or have

caused unacceptable toxicities, and where potential benefits outweigh the risks of toxicities.

- Didanosine plus zalcitabine or stavudine plus zalcitabine: These combinations are contraindicated due to increased rates and severity of peripheral neuropathy.
- Efavirenz in first trimester of pregnancy and women with significant childbearing potential: Efavirenz use was associated with significant teratogenic effects in primates at drug exposures similar to those representing human exposure. Several cases of congenital anomalies have been reported after early human gestational exposure to efavirenz. Efavirenz should be avoided in pregnancy, particularly during the first trimester, and in women who are trying to conceive or who are not using effective and consistent contraception. If no other antiretroviral options are available in the woman who is pregnant or at risk for becoming pregnant, consultation should be obtained with a clinician who has expertise in both HIV and pregnancy.
- Emtricitabine plus lamivudine: Both of these drugs have similar resistance profiles and have minimal additive antiviral activity.
- Lamivudine plus zalcitabine: In vitro data showed that these two agents may inhibit intracellular phosphorylation of one another, resulting in decreased triphosphate concentration and antiretroviral activities.
- Saquinavir hard gel capsule (Invirase®) as a single PI: The hard gel formulation of saquinavir is contraindicated as a single PI due to poor bioavailability that averages only 4% even with a concurrent high-fat meal.
- Stavudine plus zidovudine: Combination regimens containing these two NRTIs should be avoided due to the demonstration of antagonism in vitro and in vivo.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- These recommendations are not intended to supersede the judgment of clinicians who are knowledgeable in the care of human immunodeficiency virus (HIV)-infected individuals.
- These guidelines generally represent the state of knowledge regarding the use of antiretroviral agents. However, as the science rapidly evolves, the availability of new agents and new clinical data may rapidly change therapeutic options and preferences.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Foreign Language Translations
Patient Resources

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Panel on Clinical Practices for Treatment of HIV Infection. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Bethesda (MD): Department of Health and Human Services (DHHS); 2004 Oct 29. 110 p. [287 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1998 Dec 1 (revised 2004 Oct 29)

GUIDELINE DEVELOPER(S)

Centers for Disease Control and Prevention - Federal Government Agency [U.S.]
Department of Health and Human Services (U.S.) - Federal Government Agency [U.S.]

SOURCE(S) OF FUNDING

United States Government

GUIDELINE COMMITTEE

Panel on Clinical Practices for Treatment of HIV Infection

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

These guidelines were developed by the Panel on Clinical Practices for Treatment of HIV Infection convened by the Department of Health and Human Services (DHHS).

Leadership of the Panel consists of John G. Bartlett (co-chair), Johns Hopkins University, Baltimore, MD; and H. Clifford Lane (co-chair), National Institutes of Health, Bethesda, MD

Current members of the Panel include: Jean Anderson, Johns Hopkins University, Baltimore, MD; A. Cornelius Baker, Whitman-Walker Clinic, Washington, DC; Samuel A. Bozzette, San Diego Veterans Affairs Medical Center, San Diego, CA; Charles Carpenter, Brown Medical School, Providence, RI; Martin Delaney, Project Inform, San Francisco, CA; Lawrence Deyton, Department of Veterans Affairs, Washington, DC; Wafaa El-Sadr, Harlem Hospital Center & Columbia University, New York, NY; Courtney V. Fletcher, University of Colorado Health Sciences Center, Denver, CO; Gregg Gonsalves, Gay Men's Health Crisis, New York, NY; Eric P. Goosby, Pangaea Global AIDS Foundation, San Francisco, CA; Fred Gordin, Veterans Affairs Medical Center, Washington, DC; Roy M. Gulick, Weill Medical College of Cornell University, New York, NY; Mark Harrington, Treatment Action Group, New York, NY; Martin S. Hirsch, Massachusetts General Hospital and Harvard University, Boston, MA; John W. Mellors, University of Pittsburgh, Pittsburgh, PA; James Neaton, University of Minnesota, Minneapolis, MN; Robert T. Schooley, University of Colorado, Denver, CO; Renslow Sherer, Project HOPE, Midland, VA; Stephen A. Spector, University of California San Diego, La Jolla, CA; Sharilyn K. Stanley, Austin, TX; Paul Volberding, University of California San Franscisco & VA Medical Center, San Francisco, CA; Suzanne Willard, Drexel University, Philadelphia, PA

Participants from the Department of Health and Human Services include: Debra Birnkrant, Food and Drug Administration; Victoria Cargill, National Institutes of Health; Laura Cheever, Health Resources and Services Administration; Mark Dybul, National Institutes of Health (Co-Executive Secretary); Jonathan Kaplan, Centers for Disease Control and Prevention; Henry Masur, National Institutes of Health; Lynne Mofenson, National Institutes of Health; Jeffrey Murray, Food and Drug Administration; Alice Pau, National Institutes of Health (Executive Secretary)

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Jean Anderson

- Abbott (Speakers bureau, recipient of support for educational program)
- Agouron/Pfizer (Speakers' bureau, recipient of support for research and educational programs, advisory board member)
- Boehringer-Ingelheim (Recipient of support for educational program)
- Glaxo-Smith Kline (Speakers bureau, recipient of support for educational program)

A. Cornelius Baker

- None

John G. Bartlett

- Abbott (HIV Advisory Board)
- Bristol-Myers Squibb (HIV Advisory Board)

Debra Birnkrant

- None

Sam Bozzette

- Abbott (Speakers' bureau)
- Bristol-Myers Squibb (Consultant)
- EMEA Consortium (Grantee)
- Roche (Grantee)

Victoria Cargill

- None

Charles Carpenter

- None

Laura Cheever

- None

Martin Delaney

- None

Lawrence Deyton

- None

Wafaa El-Sadr

- None

Mark Dybul

- None

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- Bristol-Myers Squibb (Speakers' bureau)
- Glaxo-Smith Kline (Speakers' bureau)

Gregg Gonsalves

- None

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- Gilead (Ad-hoc consultant)
- Johnson & Johnson (Grant support)
- Kaiser Family Foundation (Ad-hoc consultant)
- Pfizer/Agouron (Grant support)
- Pfizer (Grant support)

Fred Gordin

- None

Roy M. Gulick

- Abbott (Research grant, ad-hoc consultant)
- Boehringer-Ingelheim (Research grant, ad-hoc consultant)
- Bristol-Myers Squibb (Ad-hoc consultant, speaker honoraria)
- Gilead (Speaker honoraria)
- Glaxo-Smith Kline (Ad-hoc consultant)
- Merck (Research grant, speaker honoraria)
- Panacos (Ad-hoc consultant)
- Progenics (Research grant)
- Pfizer (Research grant, ad-hoc consultant)
- Roche/Trimeris (Ad-hoc consultant, speaker honoraria)
- Schering (Ad-hoc consultant)
- Tibotec (Research grant, ad-hoc consultant
- Virologic (Ad-hoc consultant)

Mark Harrington

- None

Martin Hirsch

- Bristol-Myers Squibb (Ad-hoc consultant)
- Glaxo-Smith Kline (Ad-hoc consultant)
- Millennium (Research support)
- Schering Plough (Ad-hoc consultant)
- Takeda (Research support)

Jonathan Kaplan

- None

H. Clifford Lane

- Chiron (Research support [CRADA])

Richard Marlink

- African Comprehensive HIV/AIDS Partnerships (Gates/Merck MGO) (Board of Directors)
- Secure the Future (a BMS Foundation) (Grant/research support)

Henry Masur

- Cubist (Advisory Board member)
- Gilead (Data Safety Monitoring Board [DSMB])
- Virco (DSMB)

Celia Maxwell

- Pfizer/Agouron (Support for conference)

John Mellors

- Achillion Pharmaceuticals (Stock holder)
- Boehringer-Ingelheim (Advisory Board member)
- Bristol-Myers Squibb (Research grant)
- Gilead Sciences (Advisory Board member)
- Glaxo-Smith Kline (Advisory Board member, research grant)
- Idenix Pharmaceuticals (Stock holder)
- Merck and Co., Inc. (Advisory Board member)
- Pharmasset (Stock options)
- Tibotec-Virco (Advisory Board member)

Lynne Mofenson

- None

Jeffrey Murray

- None

James Neaton

- Bristol-Myers Squibb (DSMB [non-HIV trial])
- Chiron (Research grant)
- Glaxo-Smith Kline (Speaker honoraria)
- Merck (DSMB [non-HIV trial])

James Oleske

- None

Alice Pau

- None

Robert Schooley

- Achillion (Scientific Advisory Board, stock option)
- Bristol-Myers Squibb (Consultant)
- Gilead (Consultant, Scientific Advisory Board)
- Glaxo-Smith Kline (Consultant, research support)
- Merck (Consultant, research support, Scientific Advisory Board)
- Pfizer (Consultant)
- Roche (Consultant)
- Vertex (Scientific Advisory Board, stock)
- Virologic (Scientific Advisory Board, stock options)

Renslow Sherer

- Abbott (Consultant, grant/research support, speakers' bureau)
- Agouron (Consultant, grant/research support, speakers' bureau)
- Boehringer-Ingelheim (Consultant)
- Bristol-Myers Squibb (Consultant, grant/research support, speakers' bureau)
- Chiron (Grant/research support, speakers' bureau)
- Dupont (Consultant, grant/research support, speakers' bureau)
- Gilead (Consultant, speakers' bureau)
- Glaxo-Smith Kline (Consultant, grant/research support, speakers' bureau)
- Merck (Consultant)
- Ortho-Biotech (Consultant, grant/research support, speakers' bureau)
- Roxanne (Speakers' bureau)
- Sarawak-Medichem (Grant/research support, speakers' bureau)
- Tibotec-Virco (Consultant)
- US Bioscience (Speakers' bureau)

Daniel Simpson

- None

Stephen Spector

- Bristol-Myers Squibb (Grant support)

Sharilyn Stanley

- None

Paul Volberding

- Boehringer-Ingelheim (Advisory Board)
- Bristol-Myers Squibb (Advisory Board, speaker)
- Gilead (Advisory Board, speaker)
- Glaxo-Smith Kline (Speaker)
- Immune Response (Advisory Board, stock option)
- Ortho-Biotech (Advisory Board)
- Pfizer (Advisory Board)

Suzanne Willard

- Glaxo-Smith Kline (Speaker)
- Roche (Speakers' bureau)

GUIDELINE STATUS

This is the current release of the guideline. It was last updated on October 29, 2004.

These guidelines generally represent the state of knowledge regarding the use of antiretroviral agents. However, as the science rapidly evolves, the availability of new agents and new clinical data may rapidly change therapeutic options and preferences. The guidelines are therefore updated frequently by the Panel, which meets monthly by teleconferencing to make ongoing revisions as necessary. All revisions are summarized and highlighted on the AIDSinfo Web site. Proposed revisions are posted for a public comment period, generally for 2 weeks, after which comments are reviewed by the Panel prior to finalization. Comments can be sent to aidsinfowebmaster@aidsinfo.nih.gov.

Status information regarding this guideline is available from the AIDSinfo Web site, telephone (800) 448-0440, fax (301) 519-6616; TTY (888) 480-3739.

GUIDELINE AVAILABILITY

Electronic copies: Available from the AIDSinfo Web site.

Electronic copies are also available from the National Library of Medicine's HSTAT database.

Print copies: Available from the Centers for Disease Control and Prevention, National Prevention Information Network (NPIN), P.O. Box 6003, Rockville, MD 20850. Telephone: (800) 458-5231, TTY (800)-243-7012 International number (301)-562-1098. Web site: www.cdcnpin.org.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Report of the NIH Panel to Define Principles of Therapy of HIV Infection and Guidelines for the Use of Antiretroviral Agents in HIV-Infected Adults and Adolescents. MMWR Morb Mortal Wkly Rep 1998 Apr 24;47(RR-5):43-82.
- Adherence to potent antiretroviral therapy. 2004 Oct 29. 5 p. Electronic copies: Available in Portable Document Format (PDF) from the AIDSinfo Web site.

Print copies: Available from the Centers for Disease Control and Prevention, National Prevention Information Network (NPIN), P.O. Box 6003, Rockville, MD 20850. Telephone: (800) 458-5231, TTY (800)-243-7012 International number (301)-562-1098. Web site: AIDSinfo Web site.

Print copies: Available from Southeast AIDS Training and Education Center, Emory University School of Medicine, 735 Gatewood Road, NE, Atlanta, GA 30322. Telephone: (404) 727-2929; fax (404) 727-4562. E-mail: seatec@emory.edu. Web site: www.seatec.emory.edu.

PATIENT RESOURCES

The following is available:

- HIV and Its Treatment: What You Should Know (English or Spanish) - Oct 2004.

Electronic copies: Available from the AIDSinfo Web site.

Print copies: Available from the Centers for Disease Control and Prevention, National Prevention Information Network (NPIN), P.O. Box 6003, Rockville, MD 20850. Telephone: (800) 458-5231, TTY (800)-243-7012 International number (301)-562-1098. Web site: http://www.cdcnpin.org.

NGC STATUS

This summary was completed by ECRI on July 20, 1999. The original information was verified by the guideline developer on August 10, 1999. Updated guidelines were issued on January 28, 2000, February 5, 2001, April 23, 2001, August 17, 2001, February 4, 2002, July 14, 2003, November 10, 2003, November 17, 2003, and March 29, 2004. This summary was most recently updated on November 1, 2004. This summary was updated on January 21, 2005, following the release of a public health advisory from the U.S. Food and Drug Administration regarding the use of nevirapine.

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